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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/538,036	03/29/2000	Christophe P. G. Gerald	57155-D/JPW	6128
7590	12/24/2003		EXAMINER	
John P White Cooper & Dunham LLP 1185 Avenue of the Americas New York, NY 10036			MURPHY, JOSEPH F	
			ART UNIT	PAPER NUMBER
			1646	13

DATE MAILED: 12/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No.	Applicant(s)	
	09/538,036	GERALD ET AL.	
	Examiner Joseph F Murphy	Art Unit 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1) Responsive to communication(s) filed on 21 February 2002.

2a) This action is **FINAL**.      2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

4) Claim(s) 26 and 218-235 is/are pending in the application.

4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

5) Claim(s) 218-234 is/are allowed.

6) Claim(s) 26 and 235 is/are rejected.

7) Claim(s) \_\_\_\_\_ is/are objected to.

8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.

    Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

    Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. §§ 119 and 120

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All    b) Some \*    c) None of:

    1. Certified copies of the priority documents have been received.

    2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.

    3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

    \* See the attached detailed Office action for a list of the certified copies not received.

13) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

    a) The translation of the foreign language provisional application has been received.

14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

#### Attachment(s)

1) Notice of References Cited (PTO-892)      4) Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_ .

2) Notice of Draftsperson's Patent Drawing Review (PTO-948)      5) Notice of Informal Patent Application (PTO-152)

3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5.      6) Other: \_\_\_\_\_

## **DETAILED ACTION**

### ***Formal Matters***

Claims 26, 218-235 are pending in this application. However, *ex parte* prosecution was suspended in the Office Action dated 3/10/2003 pending the availability of a reference relevant to the examination of this application. However, upon further review of this application, new issues have been raised. Therefore, the suspension of this application has been lifted and the following rejections made.

### ***Claim Objections***

Claim 26 is objected to because of the following informalities: It is dependent on cancelled claim 1. Appropriate correction is required.

### ***Claim Rejections - 35 USC § 112 first paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 26 is rejected under 35 U.S.C. 112, first paragraph, because the specification, which is enabling for a full length human NPFF2 protein of SEQ ID NO: 1, does not reasonably provide enablement for a monomer with a P-S6 region which is 80% identical to human NPFF2 P-S6 region, or a monomer which specifically binds to SEQ ID NO: 1, or a human NPFF2 amino acid sequence. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim 26 is overly broad since insufficient guidance is provided as to which of the myriad of variant encoded polypeptides which will retain the characteristics of NPFF2. The claim is directed to nucleic acids which hybridize to the nucleic acid of SEQ ID NO: 43, but the conditions under which the hybridization is carried out are not set forth (see rejection under 35 USC § 112 second paragraph, *infra*). Additionally, the claim is directed to nucleic acids which hybridize to the complement of the sequence of SEQ ID NO: 43, but there is no structural limitation set forth for this nucleic acid, such as length or homology. The claims are thus directed to variant polynucleotides encoding variant polypeptides. However, Applicants do not disclose any actual or prophetic examples on expected performance parameters of any of the possible muteins of NPFF2. It is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. For example, As an example of the unpredictable effects of mutations on protein function, Mickle et al. teaches that cystic fibrosis is an autosomal recessive disorder caused by abnormal function of a chloride channel, referred to as the cystic fibrosis transmembrane conductance regulator (CFTR) (page 597). Several mutations can cause CF, including the G551D mutation. In this mutation a glycine replaces the aspartic acid at position 551, giving rise to the CF phenotype. In the most common CF mutation, delta-F508, a single phenylalanine is deleted at position 508, giving rise to the CF phenotype. Thus showing that even the substitution or deletion of a single amino acid in the entire 1480 amino acid CFTR protein sequence can have dramatic and unpredictable effects on the function of the protein. Additionally, it is known in the art that even a single amino acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell. For example, Voet et al. (1990)

teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (pages 126-128, section 6-3A and page 230, column 2, first paragraph). Since the claims encompass variant polypeptides and given the art recognized unpredictability of the effect of mutations on protein function, it would require undue experimentation to make and use the claimed invention. See *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. While the claims set forth a functional limitation for the variant polypeptides wherein the polypeptide has the ability to form a voltage-gated potassium channel, the amino acid sequence of a polypeptide determines its structural and functional properties, and the predictability of which amino acids can be substituted is extremely complex and outside the realm of routine experimentation, because accurate predictions of a polypeptide's structure from mere sequence data are limited. Since detailed information regarding the structural and functional requirements of the polynucleotide and the encoded polypeptide are lacking, it is unpredictable as to which variations, if any, meet the limitations of the claims. Applicant is required to enable one of skill in the art to make and use the claimed invention, while the claims encompass polynucleotides which encode polypeptides which the specification only teaches one skilled in the art to test for functional variants. It would require undue experimentation for one of skill in the art to make and use the claimed polypeptides. Applicant is required to enable one of skill in the art to make and use the claimed invention, while the claims encompass polynucleotides encoding

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polypeptides that the specification only teaches one skilled in the art to test for functional variants. Since the claims do not enable one of skill in the art to make and use the claimed polypeptides, but only teaches how to screen for the claimed polynucleotides encoding polypeptides, and since detailed information regarding the structural and functional requirements of the polypeptides are lacking, it is unpredictable as to which variations, if any, meet the limitations of the claims. Thus, since Applicant has only taught how to test for polynucleotides which encode polypeptide variants of NPFF2, and has not taught how to make polypeptide variants of NPFF2, it would require undue experimentation of one of skill in the art to make and use the claimed polynucleotides.

Claim 26 is rejected, under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Claim 26 is a genus claim. The claim is directed to nucleic acids which hybridize to the nucleic acid of SEQ ID NO: 43, but the conditions under which the hybridization is carried out are not set forth (see rejection under 35 USC § 112 second paragraph, *infra*). Additionally, the claim is directed to nucleic acids which hybridize to the complement of the sequence of SEQ ID NO: 43, but there is no structural limitation set forth for this nucleic acid, such as length or homology. The claims are thus directed to variant polynucleotides encoding variant polypeptides. The specification and claim do not indicate what distinguishing attributes shared by the members of the genus. The specification and claims do not place any limit on the number of amino acid substitutions, deletions, insertions and/or additions that may be made to the encoded NPFF2 variants. Thus, the scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification and claim do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed.

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Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, SEQ ID NO: 43 is insufficient to describe the genus. The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. In the instant case, the specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the genus of polypeptides. There is no description of the conserved regions which are critical to the structure and function of the genus claimed. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Structural features that could distinguish the compounds in the genus from other seven transmembrane region compounds are missing from the disclosure. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the polynucleotides and polypeptides encompassed. Thus, no identifying characteristics or properties of the instant polypeptides are provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 26 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 26 recites the term "low stringency conditions", which is a conditional term and renders the claim indefinite. Furthermore, some nucleic acids that might hybridize under conditions of low stringency, for example, would fail to hybridize under conditions of high stringency. The metes and bounds of the claim thus cannot be ascertained. This rejection could be obviated by supplying specific conditions supported by the specification which Applicant considers to be "low stringency".

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 235 is rejected under 35 U.S.C. 102(b) as being anticipated by Lukacs et al. (1992).

Lukacs teaches the preparation of a membrane preparation, in this case endosomes, from CHO cells which comprise the CFTR protein. Claim 235 is directed to a membrane preparation isolated from, *inter alia*, CHO cells. Claim 235 as written does not contain a limitation wherein

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the membrane preparation must comprise the encoded NPFF2 protein. Therefore, the membrane preparation of Lukacs et al. anticipates the membrane preparation of claim 235 in that it is isolated from CHO cells, and is thus identical to the instantly claimed membrane preparation.

***Conclusion***

Claims 26 and 235 are rejected.

Claims 218-234 are allowable.

***Advisory Information***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph F. Murphy whose telephone number is 703-305-7245. The examiner can normally be reached on M-F 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 703-308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



Joseph F. Murphy, Ph. D.  
Patent Examiner  
Art Unit 1646  
December 8, 2003